**DOCKET NO.: PHOE-0057** 

**Application No.:** 09/504,280

Office Action Dated: February 3, 2004

**PATENT** REPLY FILED UNDER EXPEDITED

PROCEDURE PURSUANT TO 37 CFR § 1.116

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:** 

1. (Currently amended) Modified TNF, comprising a polypeptide having TNF

biological activity covalently bound to PEG molecules having an approximate weight

average molecular weight in the range of 15,000 to about 40,000 wherein said biological

activity of said polypeptide comprises the ability to kill METH A tumors in vivo.

2. (Currently amended) The modified TNF of Claim 1 wherein said PEG is covalently

bound to primary amine groups on said polypeptide having TNF biological activity through a

biocompatible linker and where said PEG has an approximate weight average molecular

weight in the range of 20,000 to about 30,000.

(Previously presented) The modified TNF of claim 24 wherein said linker is selected 3.

from the group consisting of succinimidyl succinate, succinimidyl proprionate, and N-

hydroxy succinimidyl.

4. (Original) The modified TNF of Claim 2 wherein said linker is selected from the

group consisting of succinimidyl succinate, succinimidyl proprionate, and N-hydroxy

succinimidyl.

5. (Currently amended) The modified TNF of Claim 1 wherein said polypeptide having

TNF biological activity is TNF- $\alpha$ .

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6. (Currently amended) The modified TNF of Claim 1 wherein said polypeptide having

TNF biological activity is isolated human TNF.

7. (Currently amended) The modified TNF of Claim 1 wherein said polypeptide having

TNF biological activity is recombinant human TNF.

(Currently amended) The modified TNF of Claim 1 wherein said polypeptide having 8.

TNF biological activity is human TNF mutated by deleting amino acids 1-9 of the mature

TNF protein.

9-13. (Canceled)

(Currently amended) A method of enhancing the circulating half life of a polypeptide 14.

having TNF biological activity while reducing its toxicity comprising modifying said

polypeptide having TNF biological activity by covalently bonding to it PEG molecules

having an approximate weight average molecular weight in the range of 15,000 to about

40,000 wherein said biological activity of said polypeptide comprises the ability to kill

METH A tumors in vivo.

(Currently amended) The method of Claim 14 in which said PEG is covalently bound 15.

to primary amine groups on said polypeptide having TNF biological activity through a

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biocompatible linker and where said PEG has an approximate weight average molecular

weight in the range of 20,000 to about 30,000.

16. (Currently amended) A method of enhancing the tumoricidal activity of a polypeptide

having TNF biological activity comprising modifying said polypeptide having TNF

biological activity by covalently bonding to it PEG molecules each molecule having an

approximate molecular weight of 20,000 to 30,000 wherein said biological activity of said

polypeptide comprises the ability to kill METH A tumors in vivo.

17. (Currently amended) The method of Claim 16 in which said PEG is covalently bound

to primary amine groups on said polypeptide having TNF biological activity through a

biocompatible linker and where said PEG has an approximate weight average molecular

weight in the range of 20,000 to 30,000.

18-23. (Canceled)

24. (Currently amended) The modified TNF of claim 1 wherein said PEG is covalently

bound to primary amine groups on said polypeptide having TNF biological activity through a

biocompatible linker.

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